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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/981,215	10/16/2001	Janice K. Albrecht	IN01344	5760

24265 7590 06/28/2005

SCHERING-PLOUGH CORPORATION
PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER	
FOLEY, SHANON A	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 06/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/981,215	ALBRECHT, JANICE K.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/18/5*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

The request filed on 5/18/2005 for a Request for Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/981,215 is acceptable and a RCE has been established. An action on the RCE follows.

In the amendment submitted May 18, 2005, applicant amended claims 20, 29 and added new claims 43-46.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The amendment to claim 29 renders the claim confusing. It is not clear from the amendment notation what is intended to be deleted. Since "greater than 10.6 mg/kg of the patient's body weight" is underlined, it is presumed that this clause is to be deleted. If this is what is intended, the claim reads, "...administering to the patient of ribavirin per day...", which does not make grammatical sense. Since "greater than" is new to the claim, the claim will be interpreted in view of this amount of ribavirin in relation to the patient's body weight in the interest of compact prosecution. However, this treatment does not remedy the confusion in the claim. This rejection also affects claims 30-45.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 20-42 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-70 of U.S. pre-grant publication no. US 2003/0039630 A1 for reasons of record.

Claims 20 and 29 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3-7 of U.S. pre-grant publication no. US 2002/0055473 for reasons of record.

New claims 43-46 fall within the scope of previously presented claims and are also rejected on the same grounds as the previously presented claims. Applicant addresses each of the rejections above separately and states that a terminal disclaimer will be filed to obviate the provisional double patenting rejections upon indication of allowable subject matter. Until the terminal disclaimers are received, the rejections will be maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 20-46 are rejected under 35 U.S.C. 102(a) as being anticipated by Glue et al. (WO 00/37110) for reasons of record.

New claims 43 and 44 fall within the scope of the previously pending claims (i.e. a person weighing 60-65 kg would be administered about 800 mg/day of ribavirin, which is equivalent to administering 13-14.5 mg/kg of ribavirin). In addition, claims 45 and 46 specify that the patient is a treatment naïve patient and Glue et al. teach this limitation, see claim 21 for example.

Applicant argues that Glue et al. differ from the claimed invention because the reference teaches the administration of ribavirin and interferon during two treatment periods.

In response, the instant claims require administering ribavirin and interferon for "a treatment time period sufficient", which encompasses any treatment regiment.

Applicant notes that the proposed ribavirin dosage regiment of Glue et al. was likely a typographical error. Applicant concludes that the teachings of Glue et al., at best, suggest trying interferon/ribavirin using 1000-1200 mg/kg/day of ribavirin. However, this argument is speculative and unsupported since Glue et al. specifically teach administering 400-1200 mg/day of ribavirin to a chronically infected HCV patient, see claim 22 for example.

Applicant asserts that Glue et al. do not discuss the weight range of the patients to be included in the planned studies. Applicant also states that there is no suggestion in Glue et al. to adjust the dose of both the pegylated interferon and ribavirin based on a patient's weight to improve treatment efficacy.

Applicant's arguments have been fully considered, but are found unpersuasive. The instant claims are drawn to a method of treating a patient having a chronic hepatitis C infection by administering 800-1200 mg/kg/day of ribavirin and 1.5 μg/kg of pegylated interferon alfa-2b once a week for a time period sufficient to eradicate detectable HCV-RNA levels for at least 12 weeks after the end of the treatment period. Glue et al. clearly anticipate a method of treating a patient having a chronic hepatitis C infection by administering 400-1200 mg/day of ribavirin and 1.5 μg/kg of pegylated interferon alfa-2b once a week for a time period sufficient to eradicate detectable HCV-RNA levels for at least 24 weeks after the end of the treatment period, see claims 1-25 and page 3, line 3 to page 4, line 3. Therefore, Glue et al. anticipate the method claimed. Glue et al. clearly indicate that the weight of an individual is a factor for determining the concentration of drugs to be administered since .05 to 1.5 micrograms per kilogram of interferon is administered (emphasis added), see claims 9-14 and 22-25. Therefore, Glue et al. anticipate the dosage range required of ribavirin and interferon to treat any chronically HCV-infected individual, regardless of weight. Further, MPEP § 2144.05 states that "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical"...and... "where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)". However, in the instant case, there is no difference between the concentrations of ribavirin and interferon administered and the concentrations administered by Glue et al. Therefore, it is maintained that Glue et al. anticipate the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 20-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davis et al. (reference AN provided in the IDS) and Gilbert (WO 95/13090) for reasons of record.

Claims 20-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over McHutchison et al. (reference AM of the IDS) and Gilbert (WO 95/13090) for reasons of record.

Claims 20-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Poynard et al. (provided in the IDS as AL) and Gilbert (WO 95/13090) for reasons of record.

Claims 20-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reichard et al. (provided in the IDS as AK) and Gilbert (WO 95/13090) for reasons of record.

As stated previously, new claims 43 and 44 fall within the scope of ribavirin administered in the previously pending claims. In addition, claims 45 and 46 specify that the patient is a treatment naïve patient. McHutchison et al. or Poynard et al. or Reichard et al. each, in the alternative, teach this limitation, see the "Selection of Patients" of McHutchison et al., "Patients" of Poynard et al., and "Methods" section of Reichard et al., respectively.

For all of the rejections under 35 USC § 103, applicant argues that none of the references teach or suggest the particular combination of weight-based dosages of pegylated interferon and ribavirin.

A review of the references in view of applicant's arguments have been considered, but are found unpersuasive. Contrary to applicant's assertion, Davis et al. teach treating chronic HCV by administering 1000 or 1200 mg per day of ribavirin, depending on body weight, and 3 million units of interferon three times a week (emphasis added). Alternatively, McHutchison et al. teach treating chronic HCV by administering 1000 or 1200 mg per day of ribavirin, depending on body weight, and 3 million units of interferon three times a week (emphasis added). Poynard et al. teach treating chronic HCV by administering 1000 or 1200 mg per day of ribavirin and 3 million units of interferon three times a week. Finally, Reichard et al. teach treating chronic HCV by administering 1000 or 1200 mg per day of ribavirin and 3 million units of interferon three times a week. Although neither Poynard et al. nor Reichard et al. mention body weight for administration, it is maintained that either reference specifically teach amount of ribavirin claimed to be administered.

Applicant further argues that the teachings in the references amount to "obvious to try" and that the rejection relies on impermissible hindsight to arrive at the particular dosages of ribavirin and interferon claimed. Applicant argues that there is no motivation for the ordinary artisan to derive a dose of 1200 mg/day for a patient that weighs more than 85 kg or administer an amount of ribavirin that is greater than 10.6 mg/kg/day.

Applicant's arguments and a review of the references have been fully considered, but are found unpersuasive. Contrary to applicant's assertion regarding the lack of motivation to arrive at a dose of 1200 mg/day of ribavirin, Davis et al. or McHutchison et al. or Poynard et al. or Reichard et al., respectively, explicitly teach administering 1200 mg/day of ribavirin in a possible dose ranging from 1000-1200 mg/day.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case, the claims are drawn to a method of treating a patient having a chronic hepatitis C infection by administering 800-1200 mg/kg/day of ribavirin and 1.5 μg/kg of pegylated interferon alfa-2b once a week for a time period sufficient to eradicate detectable HCV-RNA levels for at least 12 weeks after the end of the treatment period. Davis et al. or McHutchison et al. or Poynard et al. or Reichard et al., respectively, teach a method of treating chronic HCV by administering 1000 or 1200 mg per day of ribavirin and 3 million units of interferon three times a week. The dosage mount of ribavirin taught by each of the references is equivalent to the dosage of ribavirin instantly claimed for administration. Further, Davis et al., or alternatively, McHutchison et al. clearly indicate that the weight of an individual is a factor for determining the concentration of drugs to be administered since 1000 or 1200 mg per day of ribavirin, depending on body weight, is administered (emphasis added). Davis et al. or McHutchison et al. or Poynard et al. or Reichard et al., respectively, teach the instant dosage of ribavirin to be administered, regardless of weight. It is conventional practice in the vaccine art to optimize dosages, depending on individual factors for each patient, i.e. weight. Further, MPEP § 2144.05 states that "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is

evidence indicating such concentration or temperature is critical"...and... "where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)". In the instant case, there is no difference between the concentrations of ribavirin administered and the concentrations administered in the instant claims.

Applicant also asserts that the comparison between the dosage units of interferon administered in the prior art and the dosage unit instantly claimed would be relevant for an anticipation by inherency rejection rather than an obvious-type rejection.

However, the inherency argument between the dosage unit used in the art and the unit instantly claimed is proper under 35 USC § 103, see MPEP § 2112:

> The express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103. "The inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and obviousness." *In re Napier*, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir. 1995) (affirmed a 35 U.S.C. 103 rejection based in part on inherent disclosure in one of the references). See also *In re Grasselli*, 713 F.2d 731, 739, 218 USPQ 769, 775 (Fed. Cir. 1983).

Applicant states that since there is no direct translation to convert 3 MU of interferon to the equivalent amount in μg/kg, there is no reasonable expectation that the particular pegylated interferon would produce the claimed antiviral response with the weight-based ribavirin dose instantly claimed. Applicant also argues that there is no reasonable expectation of success that the combination of ribavirin and *pegylated* interferon instantly claimed would be effective.

Applicant's arguments have been fully considered, but are found unpersuasive. Although the dose of interferon administered by Davis et al. or McHutchison et al. or Poynard et al. or Reichard et al. is in different units, the amount administered in the references is equivalent to the

species within the range claimed since HCV RNA levels were undetectable in the method of Davis et al. or McHutchison et al. or Poynard et al. or Reichard et al. 24 weeks after the end of the treatment period and the instant claims require undetectable levels of HCV RNA for at least 12 weeks after the treatment period. Therefore, the Office has provided a rationale and evidence to support the conclusion that the interferon dosage unit taught in the art at the time the invention was made is equivalent to the dosage unit of interferon claimed.

The only difference between the teachings of Davis et al. or McHutchison et al. or Poynard et al. or Reichard et al. and the instant claims is the use of pegylated interferon instead of non-pegylated interferon. However, Gilbert et al. disclose that pegylated forms of interferon alpha retain all of the biological activity as the unconjugated forms, and are longer acting, see page 12. Applicant even admits at the top of page 11 of the response that the combination of primary references with the teachings of Gilbert et al. suggest replacing the non-pegylated interferon with pegylated interferon. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to use the pegylated interferon of Gilbert in the method of Davis et al. or McHutchison et al. or Poynard et al. or Reichard et al., respectively, to increase the duration of activity. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for substituting a pegylated form for non-pegylated form because the functional activity is the same. Additionally, one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for treating chronic HCV in the method of Davis et al. or McHutchison et al. or Poynard et al. or Reichard et al. using the pegylated interferon of Gilbert et al. because Davis et al. or McHutchison et al. or Poynard et al. or Reichard et al. individually teach undetectable levels of

HCV RNA for at least 24 weeks after the treatment period using a combination of interferon and ribavirin and Gilbert et al. teach that the functional activity of pegylated and non-pegylated forms of interferon are the same. Therefore, it is maintained that the invention as a whole would have been prima facie obvious to one of ordinary skill in the art, absent unexpected results to the contrary.

Conclusion

This is a continuation of applicant's earlier Application No. 09/981,215. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-F 6:00 AM - 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shanon Foley
Primary Examiner
Art Unit 1648